Remarks

Claims 1-25 are pending. New claims 26, 27, and 28 have been added. Therefore, claims 1-28 are under consideration. Claims 1 and 18 have been amended. Applicants have amended claims 1 and 18 to recite "wherein the nutritional supplement is administered to the subject for at least seven days prior to the onset of hypertension." Support for amended claims 1 and 18 can be found throughout the specification and at least in paragraphs 45 and 47 of example I on page 5 of the published application, where the administration of the nutritional supplement for 7 days prior to the onset of hypertension is discussed. Support for new claim 26 can be found at least on page 4, paragraph 43 where parenteral administration of the nutritional supplement is discussed. Support for new claims 27 and 28 can be found at least on page 5, paragraph 43 where one daily dose of the nutritional supplement is discussed. Applicants believe that no new matter was created by these amendments. Moreover, Applicants believe that no new issues are raised by these amendments. In particular, applying the rules of claim construction, because claims 8 and 9 are limited to oral administration and claim 1 is not so limited, claim 1 must include all the features of claim 26 and thus parenteral administration of quercetin has been considered.

35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-25 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. In particular, the Examiner alleges that "while being enabling for delaying the onset or slowing the progression of hypertension in a subject, does not reasonably provide enablement for the prevention of the hypertension." Applicants respectfully traverse this rejection.

Applicants respectfully remind the Examiner that the standard for enablement is whether the claimed invention coupled with the information known in the art enables one of skill in the art to make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir.1988). Furthermore, with respect to determining undue experimentation, "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation

should proceed." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

In determining whether experimentation is undue, the Federal Circuit in *In re Wands* provided a non-exclusive list of factors for determining undue experimentation including 1) the breadth of the claims; 2) the nature of the invention; 3) the state of the prior art; 4) the level of one of ordinary skill; 5) the level of predictability in the art; 6) the amount of direction provided by the inventor; 7) the existence of working examples; and 8) the quantity of experimentation needed to make or use the invention based on the disclosure. Here, the claims are drawn to "methods for preventing or delaying the onset of or slowing the progression of hypertension in a subject." As the Examiner has conceded that Applicants have enabled delaying the onset and slowing the progression of hypertension, only the prevention of hypertension need be addressed (see page 2, first paragraph of the present office action). Applicants note that the Examiner points to paragraph 72 of the present application as indicating that hypertension was not prevented. Applicants respectfully note that nowhere in paragraph 72 can such conclusions be drawn as that paragraph describes a method used and no results are discussed. Moreover, as noted in Figure 5, the systolic and diastolic pressure of the quercetin treated rats never rose beyond a statistical amount over the baseline measurement. Applicants also note that Figure 1 shows that rats that received nutritional supplement before abdominal aorta constriction showed no increase in arterial pressure relative to mock controls. Furthermore, Applicants show that prior treatment with quercetin resulted in the prevention of Akt activation and a reduction of ERK1/2 which is relevant as Akt activation and increase in ERK1/2 have been implicated in cardiac hypertrophy (see Figure 4 and the corresponding legend in paragraph 15). Accordingly, Applicants have indeed prevented hypertension contrary to the assertions of the Examiner and provided sufficient guidance and examples to enable the scope of the invention. Therefore, although the prior art was unable to prevent hypertension, this is negated by the fact that Applicants have provided working examples and full direction how to achieve this result. The Applicants believe this rejection to be overcome and respectfully request its withdrawal.

35 U.S.C. § 102

The Examiner has rejected claims 1-3, 7, 8, 10, and 14-16 under 35 U.S.C. § 102(b) as allegedly being anticipated by Duarte et al. (2001) *Br. J. of Pharm* 133: 117-124. In particular,

the Examiner contends that Duarte et al. disclose "oral administration of 10mg/kg of quercetin in 1% methylcellulose which lowered blood pressure and reduced left ventricular weight compared to controls." It is a long established tenet of patent law that in order for a reference to anticipate the claim, it must teach each and every limitation of the claim. Applicants respectfully point out that, as amended, claim 1 is drawn to "A method for preventing or delaying the onset of or slowing the progression of hypertension in a subject, said method comprising administering to a subject a nutritional supplement ...wherein the nutritional supplement is administered to the subject for at least seven days prior to the onset of hypertension." Respectfully, Duarte et al. does not teach the administration of quercitin prior to the onset of hypertension as is now claimed. The disclosure in Duarte administers quercetin after the onset of hypertension (at 12 weeks of age; see page 118, first line). In fact, given that the rat model used in Duarte et al was the spontaneously hypertensive rat, the administration of quercetin before the onset of hypertension would be impossible if not administered prior to 5-6week period as the hypertensive phenotype is present from that point forward. For at least these reasons, Duarte et al. fails to teach all the limitations of the claims. Therefore, Duarte et al. does not anticipate claims 1-3, 7, 8, 10, and 14-16. Applicants believe this rejection has been overcome and respectfully request its withdrawal.

35 U.S.C. § 103

The Examiner has rejected claims 1-25 under 35 U.S.C. § 103(a) as being unpatentable over Duarte et al. in view of Wakat (U.S. Patent No. 6,054,128) and Schmitz et al. ((U.S. Patent No. 6,610,320). Applicants respectfully traverse the rejection. In the recent KSR Int'l Co. v Teleflex, Inc. ruling, the Supreme Court has reaffirmed the *Graham* factors for determination of obvious under 35 U.S.C. 103(a). *KSR Int 'l Co. v. Teleflex, Inc. (KSR),* No 04-1350 (U.S. Apr. 30, 2007). The three factual inquiries under *Graham* require examination of: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art. *Graham v. John Deere (Graham),* 383 U.S. 1, 17-18, 149 USPQ 459, 467 (1966). Additionally, the court in Graham noted a fourth consideration for the determination of obviousness would be any objective evidence of secondary considerations such as unexpected results, unmet need in the art, and commercial success. Furthermore, in order to establish a prima facie case of obviousness, the examiner has the initial burden of supporting

the conclusion of non-obviousness. In particular, the Examiner has the initial burden of ascertaining the differences between the claims and the prior art which requires interpreting both the art and the claims as a whole. Put another way, "all words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Applicants respectfully assert that the prior art alone or in combination does not teach all the limitations of the claims. As Applicants have demonstrated above, Duarte et al. does not teach all limitations of the claim. Specifically, Duarte et al. does not disclose the administration of a nutritional supplement at least seven days prior to the onset of hypertension. Therefore, the Examiner must rely on the combination of Wakat and Schmitz to disclose this deficiency. The Examiner cites Wakat for the alleged teaching of "the combination of quercetin with other nutrients." Applicants respectfully note that Wakat, as with Duarte, does not disclose let alone teach the administration of a nutritional supplement comprising quercetin at least seven days prior to the onset of hypertension. Regarding Schmitz et al., Applicants respectfully note that nowhere in Schmitz et al. is disclosed the administration of quercetin let alone the administration of quercetin at least seven days prior to the onset of hypertension. Specifically, Applicants note that Schmitz et al. relates to the treating or prevention of atherosclerosis through the use of catechin not quercetin as is claimed herein. Moreover, as with the other cited references, Schmitz et al. does not disclose the prior administration of a nutritional supplement comprising quercetin at least seven days before the onset of hypertension. Furthermore, as quercetin and catechin are different chemical compounds it would be scientifically improper to assert any finding related to one upon the other. Thus, alone or in combination, the cited art fails to disclose all the limitations of the claims which is necessary to establish an claim of obviousness when the claim as a whole is considered. Accordingly, Applicants believe that the Examiner has not met the necessary requirements to establish a prima facie case of obviousness. Applicants believe this rejection has been overcome and respectfully request its withdrawal.

Pursuant to the above remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A credit card payment in the amount of $525.00 is being submitted electronically, representing the small-entity fee for a three (3) month Extension of Time under 37 C.F.R. § 1.17(a)(3), and a Request for a three (3) month Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,
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CERTIFICATE OF EFS-WEB TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being transmitted by EFS-WEB on the date indicated below.

J. Gibson Lanier, Ph.D.

Date 4/9/08